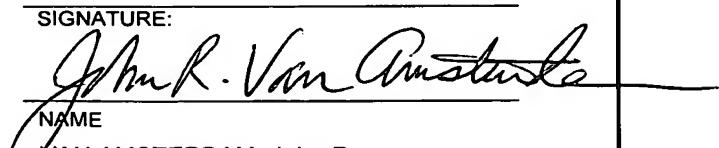


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| <b>TRANSMITTAL LETTER TO THE UNITED STATES<br/>DESIGNATED/ELECTED OFFICE (DO/EO/US)<br/>CONCERNING A SUBMISSION UNDER 35 U.S.C. 371</b>  |  | ATTORNEY'S DOCKET NUMBER<br><b>B0662.70057US01</b>             |
| INTERNATIONAL APPLICATION NO.<br><b>PCT/US2004/029437</b>  | INTERNATIONAL FILING DATE<br><b>09 September 2004 (09.11.2004)</b> | PRIORITY DATE CLAIMED<br><b>09 September 2003 (09.11.2003)</b> |
| TITLE OF INVENTION <b>TUMOR SUPPRESSOR LKB1 KINASE DIRECTLY ACTIVATES AMP-ACTIVATED KINASE</b>   |  |  |
| APPLICANT(S) FOR DO/EO/US <b>CANTLEY, Lewis C.; SHAW, Reuben, J.; BARDEESY, Nabeel; DEPINHO, Ronald A.</b>   |  |  |
| Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:  |  |  |
| <ol style="list-style-type: none"> <li><input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a submission under 35 U.S.C. 371.</li> <li><input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a submission under 35 U.S.C. 371.</li> <li><input type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371 (f)). The submission must include items (5), (6), (9) and (21) indicated below.</li> <li><input type="checkbox"/> The US has been elected (Article 31).</li> <li><input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371 (c)(2))           <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> has been communicated by the International Bureau.</li> <li>c. <input checked="" type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li> </ol> </li> <li><input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371 (c)(2))           <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto.</li> <li>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).</li> </ol> </li> <li><input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))           <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> have been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. <input checked="" type="checkbox"/> have not been made and will not be made.</li> </ol> </li> <li><input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).</li> <li><input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).</li> <li><input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).</li> </ol> |  |  |
| Items 11 to 20 below concern document(s) or information included:  |  |  |
| <ol style="list-style-type: none"> <li>11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</li> <li>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li> <li>13. <input checked="" type="checkbox"/> A preliminary amendment.</li> <li>14. <input checked="" type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.</li> <li>15. <input type="checkbox"/> A substitute specification.</li> <li>16. <input type="checkbox"/> A power of attorney and/or change of address letter.</li> <li>17. <input checked="" type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821 - 1.825.</li> <li>18. <input type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 154(d)(4).</li> <li>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</li> <li>20. <input type="checkbox"/> Other items or information: PCT/IB301/304/308 (2) Forms; PCT Published Application; PCT Request Form</li> </ol>   |  |  |
| Express Mail No: EV717505815US   |  |  |

|   |              |   |  |  |        |
|---|--------------|---|--|--|--------|
| U.S. APPLICATION NO. (if known, see 37 CFR 1.5)<br><i>001571242</i>   |              | INTERNATIONAL APPLICATION NO.<br>PCT/US2004/029437                            |  | ATTORNEY'S DOCKET NUMBER:<br>B0662.70057US01 |        |
| The following fees have been submitted  |              |   |  | CALCULATIONS                                 |        |
| 21. <input checked="" type="checkbox"/> Basic national fee (37 CFR 1.492(a)).....\$300  |              |   |  | \$ 300.00                                    |        |
| 22. <input checked="" type="checkbox"/> Examination fee (37 CFR 1.492(c))<br><br>If the written opinion prepared by the ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4) .... \$ 0<br>All other situations ..... \$200   |              |   |  |  |        |
| 23. <input checked="" type="checkbox"/> Search fee (37 CFR 1.492(b))<br><br>If the written opinion of the ISA/US or the International preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4) .... \$ 0<br>Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority ..... \$100<br>International Search Report prepared by an ISA other than the US and provided to the Office or previously communicated to the US by the IB..... \$400<br>All other situations ..... \$500   |              |   |  | \$ 200.00                                    |        |
| TOTAL OF 21, 22 and 23 =  |              |   |  | \$ 600.00                                    |        |
| <input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.  |              |   |  |  |        |
| Total Sheets  | Extra sheets | Number of each additional 50 or fraction thereof (round up to a whole number) |  | RATE   |        |
| - 100 =   | /50 =        |   |  | x \$250.00                                   |        |
| Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).   |              |   |  | \$   |        |
| CLAIMS  |              |   |  | NUMBER FILED                                 |        |
| Total claims  |              |   |  | 9 - 20 =                                     | 0      |
| Independent claims  |              |   |  | 2 - 3 =                                      | 0      |
| MULTIPLE DEPENDENT CLAIM(s) (if applicable)   |              |   |  | +  | 360.00 |
|   |              |   |  | TOTAL OF ABOVE CALCULATIONS = \$ 600.00      |        |
| <input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by ½.   |              |   |  | \$ 300.00                                    |        |
|   |              |   |  | SUBTOTAL = \$ 300.00                         |        |
| Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).  |              |   |  | +  |        |
|   |              |   |  | TOTAL NATIONAL FEE = \$ 300.00               |        |
| Fee for recording the enclosed assignment (37 CFR 1.21 (h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property   |              |   |  | +  |        |
|   |              |   |  | TOTAL FEES ENCLOSED = \$ 300.00              |        |
|   |              |   |  | Amount to be refunded:                       | \$     |
|   |              |   |  | Amount to be charged:                        | \$     |
| <p>a. <input checked="" type="checkbox"/> A check in the amount of \$ 300.00 to cover the above fees is enclosed.</p> <p>b. <input type="checkbox"/> Please charge my Deposit Account No. 23/2825 in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23/2825. A duplicate copy of this sheet is enclosed.</p> <p>d. <input type="checkbox"/> Fees are to be charged to a credit card. <b>WARNING: Information on this form may become public. Credit card information should not be included on this form.</b> Provide credit card information and authorization on PTO-2038.</p> |              |   |  |  |        |
| NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the International Application to pending status.   |              |   |  |  |        |
| SEND ALL CORRESPONDENCE TO:   |              |   |  |  |        |
| Wolf, Greenfield & Sacks, P.C.<br>600 Atlantic Avenue<br>Boston, Massachusetts 02210-2206<br>Tel. (617) 646-8000  |              |   |  |  |        |
| CUSTOMER NUMBER: 23628  |              |   |  |  |        |
| SIGNATURE:    |              |   |  |  |        |
| NAME: VAN AMSTERDAM, John R.  |              |   |  |  |        |
| REGISTRATION NUMBER 40,212  |              |   |  |  |        |